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08/805,813	02/26/97	MITSUHARA	I 085760-000

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 EXAMINER

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 08/805,813	Applicant(s) Ichiro Mitsuhashi, et al.
Examiner Amy Nelson	Group Art Unit 1649



- Responsive to communication(s) filed on Feb 26, 1997.
- This action is FINAL.
- Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- Claim(s) 1-20 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- Claim(s) _____ is/are allowed.
- Claim(s) 1-20 is/are rejected.
- Claim(s) _____ is/are objected to.
- Claims _____ are subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) _____.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- *Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). 3
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Priority

1. Applicant claims priority to Japanese Patent 8-068809, filed 3/25/96, and Japanese Patent 8-187763, filed 7/17/96. Certified copies of both patents have been received, however an English translation has only been received for the 8-068809 patent, and therefore priority to the 8-187763 patent can not be considered.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

3. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to a recombinant gene comprising the sarcotoxin 1a gene and/or the hinge region from a chitinase gene and a plant gene, an expression cassette or an expression vector comprising said recombinant gene, and a transgenic plant with resistance to pathogenic bacteria and/or fungi which is transformed with said recombinant gene, said expression vector or said expression cassette. The specification does not enable any person skilled in the art to which

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it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant claims a recombinant gene comprising a gene encoding an anti-bacterial peptide, the hinge region from a chitinase gene and a plant gene, as well as an expression cassette and an expression vector comprising said recombinant gene. Applicant also claims a plant which confers resistance to pathogenic fungi and/or bacteria which comprises a gene encoding an anti-bacterial peptide and or the hinge region from a tobacco chitinase and a plant gene.

Applicant teaches how to make a DNA construct comprising the PR-1a promoter/signal peptide operably linked to the sarcotoxin 1a gene and the PR-1a gene (PSS). Applicant also teaches how to make a DNA construct futher comprising the hinge region from a tobacco chitinase gene and the PR-1a gene (PSP) (example 1). Applicant teaches transformation of tobacco with said DNA constructs and teaches detection of the expressed proteins by Western blot with anti-sarcotoxin or anti-PR1a antibodies (examples 2-3). Applicant teaches that the transformed plants have enhanced resistance to the fungal pathogens, *F. oxysporum*, *R. solani*, *P. aphanidermatum*, and *P. infestans* (examples 7-10), and to the bacterial pathogens, *P. syringae* and *E. cartovora* (examples 5-6).

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the

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invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The state of the art for modification of gene expression or of phenotypic characteristics in plants by genetic transformation is highly unpredictable and hence significant guidance is required to practice the art without undue experimentation. The specific effects of given promoters, leaders, DNA sequences, and terminator sequences on gene expression in transformed plants can not be anticipated reliably and must be determined empirically (Plant Mol. Biol. 32: 393-405, 1996, abstract, pp. 402-403). In genetically modified plants, the introduced transgenes are sometimes not expressed, and they can also result in co-suppression effects. None of these effects are predictable, and the mechanisms of gene silencing are still not fully understood (Ann. Bot. 79: 3-12, 1997, abstract, p. 9). Moreover, the phenotypic characteristics that will result from expression of a given DNA construct can not be reliably predicted. In fact, often the expected phenotypic result is not achieved. For example, antisense expression of polygalacturonase gene in transgenic tomato had no effect on fruit softening (Nature 334: 724-726, 1988, p. 725).

Given the unpredictability in the art, the instant invention is not enabled given the lack of guidance in the specification with regard to what DNA constructs, comprising what promoter and other regulatory sequences and what other genes encoding an anti-bacterial peptide confer resistance to fungal and/or bacterial pathogens in transgenic plants. Applicant teaches only how to transform tobacco plants with the disclosed DNA constructs comprising the sarcotoxin 1a gene and provides no guidance for other anti-bacterial genes that could be used in the instant invention

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of conferring fungal and bacterial resistance on transgenic plants. In the absence of such guidance, undue trial and error experimentation would be required to screen through the myriad of different anti-bacterial genes and DNA constructs comprising said genes, and the vast number of transgenic plants, to determine how to confer resistance to fungal and/or bacterial pathogens other than by genetic transformation with the sarcotoxin 1a gene. When the *Wands* factors are weighed it is concluded that undue experimentation would be required to practice the invention, and therefore the invention is not enabled.

4. Claims 2-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At claim 2, line 1, and in subsequent dependent claims, "A" should be changed to --The-- as it refers to the claim from which it depends.

At claim 2 and claim 13, the names of the organisms should be italicized.

At claim 3, line 2, the phrase "is derived from" is indefinite because it is unclear how the peptide is derived. The phrase should be changed to --is from--.

At claim 3, line 2, and in subsequent claims, "the Diptera insect" lacks proper antecedent basis, and should be changed to --a Diptera insect--.

At claim 5, lines 1-2, the phrase "a gene encoding the anti-bacterial peptide derived from the Diptera insect" is unclear because it depends from claim 1, wherein the gene encoding a

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peptide is recited. Therefore, the phrase should be changed to --the gene encoding an anti-bacterial peptide from a Diptera insect--.

At claim 5, lines 4-6, the phrase “containing the gene encoding the anti-bacterial peptide derived from the Diptera insect” is redundant and should be omitted.

At claim 5, line 7, “the recombinant gene” lacks proper antecedent basis because alternative language is used and therefore the expression cassette of line 6 is alternative to the recombinant gene of line 4. Appropriate correction is required.

At claim 5, line 7, and in subsequent claims, the phrase “bound to” is indefinite because it is unclear how the gene is bound to the promoter. The phrase should be changed to the preferred terminology of --operably linked to--.

At claim 5, line 8, and in subsequent claims, the phrase “composed of” is indefinite because it is unclear whether open or closed claim language is intended. The phrase should be changed to --comprising--.

At claim 5, line 8, “the expression cassette” lacks proper antecedent basis because alternative language is used and therefore the expression vector of line 8 is alternative to the expression cassette of line 6. Appropriate correction is required.

At claim 5, line 9, and in subsequent claims, the phrase “linked to” is indefinite because it is unclear how the gene is linked to the promoter. The phrase should be changed to the preferred terminology of --operably linked to--. Also, it is unclear whether the vector, the cassette, or the gene is linked to the plant promoter. Appropriate correction is required.

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At claim 6, lines 1-2, "the recombinant gene which encodes the anti-bacterial peptide derived from the Diptera insect" lacks proper antecedent basis. Appropriate correction is required.

At claim 6, lines 3-4, "a hinge region of tobacco chitinase" is unclear because tobacco chitinase lacks an article, the hinge region used is from the gene and not the enzyme, and there is only one hinge region on a gene. It is recommended that the phrase be changed to --the hinge region of a tobacco chitinase gene--.

At claim 5, lines 1-2, "the Sarcotoxin 1a" lacks proper antecedent basis. Appropriate correction is required.

At claim 7, line 2, the phrase "a signal sequence of a plant protein" is unclear because the signal sequence is from the gene and not the protein. It is recommended that the phrase be changed to --a signal sequence from a plant gene--.

At claim 10, line 2, the term "has" is inappropriate because it signifies closed claim language. Therefore, the term should be changed to --comprises--.

At claim 11, line 2, "expressed by" should be changed to the preferred terminology of --operably linked to--.

At claim 12, lines 3 and 5, and in subsequent claims, the phrase "in which ... is" is indefinite because it is unclear whether open or closed claim language is intended. The phrase should be changed to --comprising--.

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At claim 12, lines 5-6, "the recombinant gene" lacks proper antecedent basis because alternative language is used and therefore the expression cassette of line 5 is alternative to the recombinant gene of line 3. Appropriate correction is required.

At claim 12, line 7, the term "having" is inappropriate because it signifies closed claim language. Therefore, the term should be changed to --comprising--.

At claim 12, line 7, "the expression cassette" lacks proper antecedent basis because alternative language is used and therefore the gene of line 6 is alternative to the expression cassette of line 5. Appropriate correction is required.

At claim 12, lines 6-7, the phrase "a gene having the expression cassette" is indefinite because it is unclear how a gene can comprise an expression cassette. Appropriate correction is required.

At claim 18, line 2, "promoterhaving" is believed to be a typographical error and should be changed to --promoter having--.

At claim 18, lines 2-3, the phrase "having resistance to pathogenic fungi" is indefinite because it is unclear whether it refers to the plant promoter, the recombinant gene, or the expression cassette. Also, it is unclear how any of the above can have resistance to fungi. It is the transgenic plants that have resistance to fungi. Appropriate correction is required.

Claim 19 is indefinite because it is unclear how the expression vector allows introduction of the expression cassette into a plant. Appropriate correction is required.

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Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Jaynes *et al.* (U.S. Patent 5,597,945) or Broekaert *et al.* (U.S. Patent 5,538,525).

Both Jaynes and Broekert teach plants transformed with a recombinant gene that encodes an anti-bacterial/anti-fungal peptide, which plants have resistance to fungal and bacterial diseases (abstract, summary of invention). Hence, all of the limitations of claim 1 were previously disclosed by Jaynes or Broekert.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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8. Claims 1-2, 12-13, 15, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaynes *et al.* (U.S. Patent 5,597,945) or Broekaert *et al.* (U.S. Patent 5,538,525).

The teachings of Jaynes and Broekaert are described *supra*. Both Jaynes and Broekaert teach expression cassettes and expression vectors comprising said gene that encodes an anti-bacterial/anti-fungal peptide.

Neither Jaynes nor Broekaert teach said recombinant gene wherein said recombinant gene further comprises a hinge region of a tobacco chitinase gene and a plant gene. Furthermore, neither Jaynes nor Broekaert specifically teach disease resistance targeted to *R. solani*, *P. aphanidermatum* and *P. infestans*, or to *P. syringae* pv. *tabaci* or *E. carotovora* subsp. *carotovora*.

It would have been obvious to one of ordinary skill in the art to modify the invention of Jaynes or Broekaert to include a tobacco chitinase gene including the hinge region characteristic of Class I chitinases because chitinases were also known to have antimicrobial activity when expressed in transgenic plants. It also would have been obvious to produce plants with resistance to *R. solani*, *P. aphanidermatum* and *P. infestans*, or to *P. syringae* pv. *tabaci* or *E. carotovora* subsp. *carotovora*. The transgenic plants of both Jaynes and Broekaert have general disease resistance including a wide variety of fungi and bacteria, and hence one would have expected to achieve resistance to these specific organisms as well. One would have had a reasonable expectation of success given the success of Jaynes and Broekaert.

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Subject Matter Allowable over the Prior Art

9. Claims 3-11, 14 and 16-17 are deemed free of the prior art, given the unpredictability inherent in the process as stated above, and the failure of the prior art to teach or reasonably suggest a recombinant gene comprising a sarcotoxin 1a gene, a tobacco chitinase hinge region, and a plant gene, nor does the prior art teach transgenic plants with resistance to fungi and/or bacteria wherein said plants are transformed with a sarcotoxin 1a gene.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached at (703) 308-2897. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



DOUGLAS W. ROBINSON
SUPERVISORY PATENT EXAMINER
SP 1600

Amy J. Nelson, Ph.D.

March 27, 1998